UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

MYLAN PHARMACEUTICALS, INC.,

Plaintiff,

v.

TOMMY G. THOMPSON,
Secretary, United States Department of
Health and Human Services,
United States Food and
Drug Administration,

and

BRISTOL-MYERS SQUIBB CO.,

Defendants.

Civil Action No.: 00-2876 (RMU)

Document Nos.: 3, 4

M E M O R A N D U M O P I N I O N

GRANTING THE PLAINTIFF'S REQUEST FOR A PRELIMINARY INJUNCTION

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I. INTRODUCTION

Mylan Pharmaceuticals, Inc., a generic drug manufacturer, moves for a preliminary injunction ordering defendant Bristol-Myers Squibb Co. ("Bristol" or "BMS") to de-list U.S. Patent No. 5,150,365 ("the '365 patent") from the United States Food and Drug Administration ("FDA")'s "Orange Book" and directing the FDA to approve immediately Mylan's Abbreviated New Drug Application ("ANDA") No. 75-252. Bristol's '365 patent covers a method of using BuSpar®, Bristol's brand-name buspirone hydrochloride ("buspirone") product. Mylan seeks this preliminary injunction so that it may proceed with plans to sell its generic buspirone product. For the reasons that follow, the court will grant Mylan's request for a preliminary injunction.

II. STATUTORY FRAMEWORK: THE HATCH-WAXMAN ACT

A. Pioneer Makers and New Drug Applications (NDAs)

An understanding of the statutory and regulatory framework governing the approval of generic drugs is critical to assessing the merits of the parties' claims. The Federal Food, Drug, and Cosmetic Act ("FFDCA"), as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, authorizes the FDA to regulate the production, distribution, and sale of drugs in the United States. *See* 21 U.S.C. §§ 321-397. An applicant seeking to market a new brand-name drug ("a pioneer maker") must prepare a rigorous New Drug Application ("NDA") for FDA consideration. *See* 21 U.S.C. § 355. The NDA contains reports of the drug's safety and effectiveness, a list of the articles used as components in the drug, a statement of the composition of the drug, a description of the methods, facilities and controls used in the manufacture, processing and packaging of the drug, samples of the drug or components, if necessary, and samples of the proposed labeling. *See* 21 U.S.C. § 355(b)(1). In addition, the NDA must contain information on any patents that claim the drug or a method of using the drug and for which a claim of patent infringement could reasonably be asserted against an unauthorized party. *See* 21 U.S.C. §§ 355(b)(1), (c)(2).[1]

Upon approval of the NDA, the FDA publishes any claimed patents for the approved drug in "Approved Drug Products with Therapeutic Equivalence Evaluations," also known as the "Orange Book." *See* 21 U.S.C. § 355(j)(7)(A)(iii). Pioneer makers have considerable incentive

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[1] FDA regulations define the types of patents that may be submitted in conjunction with an NDA: drug substance (active ingredient) patents; drug product (formulation and composition) patents; and method-of-use patents. *See* 21 C.F.R. § 314.53(b). For patents covering the formulation, composition, or method of using a drug, the NDA applicant also must submit a signed declaration stating that the patent covers the formulation, composition, or use of the product described in the pending or approved application. *See* 21 C.F.R. § 314.53(c)(2).

to cause the FDA to list patents in the Orange Book. *See* Mylan's Memorandum of Law in Support of its Motion for Preliminary Injunction ("Mot. for Prelim. Inj.") at 12 (citing *Bristol-Myers Squibb Co. v. Ben Venue Labs.*, 90 F. Supp.2d 522, 524 (D.N.J. 2000)). When the FDA lists a patent for an approved drug, generic makers often have to wait an additional thirty months to obtain FDA approval of their competing generic drugs. *See* Mot. for Prelim. Inj. at 12.

B. Generic Makers and the Abbreviated-New-Drug-Application (ANDA) Process

Generic drugs are versions of brand-name prescription drugs that typically contain the same active ingredients but not necessarily the same inactive ingredients as the brand-name original. *See United States v. Generix Drug Corp*., 460 U.S. 453, 454-55 (1980); *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1062 (D.C. Cir. 1998). Before 1984, a company that wished to make a generic version of an FDA-approved brand-name drug ("a generic maker") had to file another NDA. Preparation of the second NDA was as time-consuming and costly as the original, because the applicant had to include new studies showing the drug's safety and effectiveness. *See Mova,* 140 F.3d at 1063. In 1984, however, Congress enacted the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act, which simplified the procedure for obtaining approval of generic drugs. *See* Pub. L. No. 98-417, 98 Stat. 1585 (1984), codified at 21 U.S.C. § 355 and 25 U.S.C. §§ 156 and 271(e).

The Hatch-Waxman Act represented Congress's efforts to strike a compromise between the competing interests of pioneer pharmaceutical companies and generic manufacturers. As Chief Judge (then Judge) Edwards of the Court of Appeals for this Circuit explained, the Hatch-

Waxman Act "emerged from Congress' efforts to balance two conflicting policy objectives: to induce name-brand pharmaceutical firms to make the investments necessary to research and develop new drug products, while simultaneously enabling competitors to bring cheaper, generic copies of those drugs to market." *Abbott Labs. v. Young*, 920 F.2d 984, 991 (D.C. Cir. 1990) (Edwards, J., dissenting on other grounds) (citations omitted), *cert. denied*, 402 U.S. 819 (1991). To this end, Title I of the Act aimed "to make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962." H.R. Rep. No. 857 (Part I), 98th Cong., 2d Sess. at 14 (1984). Title II of the Act, by contrast, favored the interests of pioneer makers by granting patent-term extensions and guaranteeing market exclusivity for innovative drug products. *See id.* at 15.

Under the Hatch-Waxman Act, Congress continues to require the pioneer maker to file an NDA, complete with safety and effectiveness data. Subsequent applicants who wish to manufacture generic versions of the original drug, however, are required to file only an Abbreviated New Drug Application ("ANDA"). *See* 21 U.S.C. § 355(j). Unlike the stringent requirements for an NDA, an ANDA applicant need not show independent evidence of the safety and efficacy of its generic drug, but instead can rely on the FDA's previous determination that the drug is safe and effective. *See* 21 U.S.C. § 355(j); 21 C.F.R. § 314.94(a)(3); *Mead Johnson Pharm. Group v. Bowen*, 838 F.2d 1332, 1333 (D.C. Cir. 1988). The ANDA innovation thus allows manufacturers to market generic copies of pioneer drugs without repeating the expensive and lengthy clinical trials otherwise required by federal law. For this reason, among others, generic drugs are generally much cheaper to the consumer than brand-name drugs. *See Ben Venue Labs.*,

Inc. v. Novartis Pharm. Corp., 10 F. Supp.2d 446, 449 (D.N.J. 1998); *see also Generix Drug Corp*., 460 U.S. at 455 n.1.

To receive approval of its ANDA, an applicant must show that its generic drug is "bioequivalent" to the listed reference drug. *See* 21 U.S.C. § 355(j)(4)(F). Bioequivalence refers to the rate at which, and the extent to which, the body absorbs the active ingredient(s) in the drug. *See id*. § 355(j)(8)(A); 21 C.F.R. § 320.1(e). In this case, the reference drug is BuSpar®, the brand of buspirone marketed by Bristol. The applicant must also show that the generic drug has the same route of administration, strength, and dosage form as the reference drug. *See* 21 U.S.C. §§ 355(j)(2)(A)(iii), (j)(4)(D)(i)-(ii); *see also* 21 C.F.R. § 314.92(a)(1) (1999) (indicating the categories of drug products for which an ANDA may be filed).

In addition, when a generic maker files an ANDA seeking approval of a generic version of a drug that is listed in the Orange Book, the applicant must certify that any patent information listed in the Orange Book does not bar FDA approval of a generic version of the drug. *See* 21 U.S.C. § 355(j)(2)(A)(vii); 21 C.F.R. § 314.94(a)(12). The Hatch-Waxman Act provides ANDA applicants with four certification options: (I) that no patent information on the drug product that is the subject of the ANDA has been submitted to the FDA; (II) that the patent has expired; (III) that the patent will expire on a stated date; or (IV) that the patent is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA applicant seeks approval. *See* 21 U.S.C. §§ 355(j)(2)(A)(vii)(I) to (IV). The court will refer to these certification clauses as Paragraph I, II, III and IV certifications, respectively. In the case of a patent that has not yet expired (such as the '365 patent), the ANDA applicant's only certification options are Paragraph III or IV certifications. *See id.*

The Hatch-Waxman Act also permits ANDA applicants to avoid certifying to a method-of-use patent if they are not seeking approval for any of the uses claimed in the patent. In that circumstance, the Act requires the ANDA applicant to make a statement to the FDA that the existing method-of-use patent does not relate to the use(s) for which the ANDA applicant seeks approval. *See* 21 U.S.C. § 355(j)(2)(A)(viii); 21 C.F.R. § 314.94(a)(12)(iii). This statement is known as a "Section viii Statement."

The timing of FDA approval of the ANDA depends in part on the type of certification. If the ANDA contains a Paragraph I or II certification, the FDA may approve the ANDA as soon as it is satisfied that the product is safe and effective. *See* 21 U.S.C. § 355(j)(5)(B)(i). If the ANDA contains a Paragraph III certification, the FDA cannot make the approval effective until the patent expires. *See* 21 U.S.C. § 355(j)(5)(B)(ii). If the ANDA contains a Paragraph IV certification, the date of approval is determined by a complicated statutory scheme under which the ANDA applicant must provide notice to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA refers. *See* 21 U.S.C. § 355(j)(2)(B)(i). This notice must include a detailed statement of the factual and legal basis for the ANDA applicant's assertion that the patent is not valid or will not be infringed by its generic product. *See id.*; 21 C.F.R. § 314.95.

A Paragraph IV certification has significant legal effects. *See Ben Venue Labs.*, 10 F. Supp.2d at 449. The patent law provides that submitting an application for an infringing product is itself an act of infringement. *See id*. (citing 35 U.S.C. § 271(e)(2)(A)). Thus, a Paragraph IV

certification automatically creates a cause of action for patent infringement.[2] *See id.* Upon receiving notice of a Paragraph IV certification, the patent holder has 45 days in which to file suit against the generic manufacturer. *See* 21 U.S.C. § 355(j)(5)(B)(iii).[3] If the patent-holder brings such an action, the FDA is prohibited from approving the generic maker's ANDA for a period of 30 months. *See id*. This 30-month stay allows the parties to litigate the patent infringement action in court. If the court hearing the infringement action decides the patent would be infringed by the product proposed in the ANDA, the FDA will not approve the ANDA until the patent expires. If, however, the court hearing the infringement action rules before the expiration of the 30-month period that the patent is invalid or not infringed, the FDA must approve the ANDA effective on the date of the court's decision. *See id.*

The statutory framework of the Hatch-Waxman Act creates the potential for costly patent litigation against the generic maker that files a Paragraph IV-certified ANDA. As an incentive to the first generic maker to expose itself to the risk of costly patent litigation, Hatch-Waxman provides that the first to file a Paragraph-IV certified ANDA ("the first filer") is eligible for a 180-

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[2] Paragraph IV certifications have occasioned more than their fair share of legal disputes. *See, e.g., Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1064 (D.C. Cir. 1998). The D.C. Circuit has described Paragraph IV as "far from a model of legislative draftsmanship." *See id*. at 1069. In other instances, district courts have described Paragraph IV's provisions as "very confusing and ambiguous" and "cumbersome." *See id*. (citing *Mova Pharm. Corp. v. Shalala*, 955 F. Supp. 128, 130 (D.D.C. 1997) and *Mylan Pharms., Inc. v. Sullivan*, No. 89-36-C(K), slip. op. at 6 (N.D. W.Va. May 5, 1989)).

[3] The statute also provides that during the 45-day period after the ANDA applicant gives notice of its Paragraph IV certification, "no action may be brought under section 2201 of Title 28 for a declaratory judgment with respect to the patent." *See* 21 U.S.C. § 355(j)(5)(B)(iii)(III).

day period of exclusivity ("the Exclusivity Incentive"). *See* 21 U.S.C. § 255(j)(5)(B)(iv), as amended by Pub. Law. No. 105-115, 111 Stat. 2296 (1997); *Mova v. Shalala*, 140 F.3d 1060, 1064 (D.C. Cir. 1998). That is, during those 180 days, the FDA will not approve any other ANDA for the same generic product. By its terms, the Exclusivity Incentive affords the first filer protection from competition from subsequent generic makers for 180 days beginning from the earlier of a commercial marketing or a court decision. *See* 21 U.S.C. § 355(j)(5)(B)(iv)(I), (II).

III. FACTUAL BACKGROUND

At the center of this dispute is a white, ovoid-rectangular, scored tablet called BuSpar®. *See* Mem. of Bristol-Myers Squibb Co. in Opp'n to Pl.'s Request for a Prelim. Inj. ("Bristol Opp'n"), Ex. 9 at 12; Fed. Defs.' Mem. in Opp'n to Pl.'s Mot. for Prelim. Inj. ("FDA Opp'n") at 8. Since 1986, Bristol has sold BuSpar®—which contains the active ingredient buspirone—as a medication to treat patients suffering from generalized anxiety disorder. *See* Mot. for Prelim. Inj. at 1. In 1999, Bristol sold more than $600 million of BuSpar®. *See id*. According to Bristol, BuSpar® "is one of those rare successes that provide[s] profits to its developer's shareholders and fund[s] research and development of new drugs—most of which are never successfully brought to market." Bristol Opp'n at 6.

Bristol received a patent covering the administration of buspirone to treat anxiety disorders in 1980, and obtained FDA approval of BuSpar® in 1986. *See* Mot. for Prelim. Inj. at 1. In addition, Bristol received a two-year extension to its 17-year patent term to compensate for the delays in regulatory approval of BuSpar®. *See id.* More recently, Bristol extended its exclusive rights over buspirone for an additional six months under the pediatric exclusivity provisions of the

FFDCA, 21 U.S.C. § 355a. *See id*.; FDA Opp'n at 9. Bristol's term of exclusivity, which was set to expire at 11:59 p.m. on November 21, 2000, has enabled it to sell BuSpar® for almost fifteen years without any competition from generic buspirone makers. *See* Mot. for Prelim. Inj. at 1.

Mylan is the nation's largest generic drug manufacturer. *See* Bristol Opp'n at 1. On September 29, 1998, Mylan submitted an ANDA to the FDA for a generic version of buspirone tablets. *See* FDA Opp'n at 9. Mylan's ANDA contained a Paragraph III certification stating that it would not market its generic product until the expiration of Bristol's patent 4,182,763 ("the '763 patent"). *See id*. The FDA "tentatively approved" Mylan's ANDA, with final approval contingent only on the expiration of Bristol's exclusivity on November 22, 2000. *See id*.; Mot. for Prelim. Inj. at 2. Anticipating the expiration of Bristol's exclusivity, Mylan took the steps necessary to put its buspirone product on the market, even loading its trucks with generic buspirone tablets for shipment beginning at 12:00 a.m. on November 22, 2000. *See* Mot. for Prelim. Inj. at 2.

Only twelve hours before Bristol's exclusivity was to expire, however, the U.S. Patent and Trademark Office ("PTO") issued patent 6,150,365 ("the '365 patent") to Bristol,[4] which Bristol immediately delivered to the FDA for listing in the Orange Book. *See id*. at 2; FDA Opp'n at 9; Bristol Opp'n at 14. Bristol also submitted a declaration to the FDA stating that the '365 patent

[4] The '365 patent resulted from an application Bristol filed with the PTO on June 6, 2000. *See* Mot. for Prelim. Inj. at 2. Bristol was able to obtain expedited issuance of its patent by filing a "petition to make special," a PTO procedure initiated by a patent applicant who wishes to expedite consideration of a patent application. *See id*. Bristol represented to the Patent Office that "in order to maintain its product position in what becomes a highly competitive market, [Bristol] requires issuance of this patent *prior to November 22, 2000*." Mot. for Prelim. Inj., Leff Decl., Ex. 1 at M156 (emphasis in original).

"is a method-of-use patent covering, among other things, a method of using BuSpar® for all of its approved indications." *See* FDA Opp'n at 9 (citing Bristol Declaration dated Nov. 21, 2000, Ex. B).[5] Bristol's submission to the FDA contained all the information required by the FDA's regulations, including the patent number, date of expiration, type of patent, a declaration that the '365 patent "covers the formulation, composition and/or method of use of BuSpar®," and an identification of the approved BuSpar® uses that are covered by the patent. *See* Bristol Opp'n at 14. As a result of the FDA's receipt of the '365 patent and accompanying declaration, the FDA did not give final approval to Mylan's ANDA (or to any other ANDAs) for generic buspirone tablets. *See* FDA Opp'n at 9-10.

The FDA's listing sparked a flurry of activity among Bristol, Mylan and other companies seeking to market a generic version of buspirone. On November 21, 2000, Bristol issued a press release regarding the '365 patent. *See* Bristol Press Release dated Nov. 21, 2000 (FDA Opp'n, Ex. C). As described in Bristol's press release, the '365 patent covers "a method of use of a metabolite produced by the administration of [buspirone]."[6] *Id.* Shortly after the FDA received

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[5] The sole claim in the '365 patent covered:

> A process for ameliorating an undesirable anxiety state in a mammal comprising systemic administration to the mammal of an effective but non-toxic anxiolytic dose of [6-hydrox-busprione] or pharmaceutically acceptable acid addition salt or hydrate thereof.

Mot. for Prelim. Inj., Ex. 3 at Col. 16, lines 27-32.

[6] A "metabolite" is a new molecule that is created after an existing pharmaceutical agent breaks down in the body. *See* Mot. for Prelim. Inj. at 5. The chemical name for the active metabolite of buspirone is 6-Hydroxy-8-[4-[4-(2-pyrimindinyl)-piperazinyl]-butyl]-8-azaspiro[4.5]-7,9-dione. *See id.* For convenience, the court will refer to the metabolite by its internal BMS designation, BMY 28674. *See id*.

the '365 patent, Mylan and Danbury Pharmacal, Inc. ("Danbury"), another company with a pending ANDA for buspirone, provided copies of the press release to the FDA. The FDA also received correspondence from Danbury, in which Danbury argued that under the Federal Circuit's ruling in *Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997), a patent for a metabolite could not "claim a listed drug" within the meaning of the statute. *See* FDA Opp'n at 11 (citing Danbury Correspondence to FDA dated Nov. 24 & 27, 2000, Ex. B). In addition, on November 22, 2000, Mylan filed a Section viii Statement with the FDA stating that the labeling of its drug in the ANDA did not claim the method-of-use covered by the '365 patent.[7] *See* FDA Opp'n at 10 (citing Mylan Correspondence to FDA dated Nov. 22, 2000, Ex. D). Mylan requested that the FDA accept its Section viii Statement and approve its ANDA immediately. *See* Mot. for Prelim. Inj. at 9.

In light of these submissions, and faced with contradictory information about the '365 patent, the FDA requested additional input from Mylan, Danbury, and Bristol. *See* FDA Opp'n at 11. According to the FDA, it read the Bristol press release as suggesting that the '365 patent covered a metabolite of buspirone. *See id.* At the same time, the Federal Circuit's *Hoechst-Roussel* decision suggested to the FDA that patents for a drug's metabolites do not "claim" the

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[7] Mylan's Section viii Statement stated as follows:

> With respect to the listed drug referred to in our [ANDA] for which information was filed [by Bristol] under subsection (b) or (c) for [the '365] patent, Mylan states that its labeling does not claim such a method of use.

Mot. for Prelim. Inj. at 9 (citing Leff Decl., Ex. 6). Mylan argues that it was "compelled" to make its Section viii Statement because, among other things, the '365 patent makes clear that it does not claim any of the currently approved methods of use of BuSpar®. *See* Mot. for Prelim. Inj. at 9.

listed drug itself. *See id.* The FDA therefore turned to Bristol for clarification as to whether the patent claimed only a metabolite of buspirone. Specifically, in a letter dated November 30, 2000, the FDA asked Bristol to provide "a declaration that the '365 patent issued by the PTO on November 21, 2000 contains a claim for an approved use of buspirone hydrochloride [the approved drug] that is separate from the claim for 6-hydroxy-buspirone [the metabolite] described in the November 21, 2000, Bristol-Myers Squibb press release." *See id*. at 11-12 (citing FDA Letter to Bristol dated Nov. 30, 2000, Ex. F). The FDA also asked Mylan and Danbury to submit additional legal analysis "to help the agency determine the impact of this Federal Circuit opinion [*Hoechst-Roussel*] on the patent listing process." *See* FDA Opp'n at 12.

The FDA requested this additional input from the parties on November 30, 2000. That same day, without responding to the FDA's request, both Mylan and Danbury filed suit in federal court. Mylan filed the instant action, naming both the FDA and Bristol as defendants. Danbury filed suit in the U.S. District Court for the District of Maryland, naming FDA Commissioner Jane Henney as the sole defendant. In both suits, the plaintiffs requested preliminary injunctive relief that would prevent the listing of the '365 patent and require the FDA to approve their buspirone ANDAs immediately. (The Maryland litigation is discussed in greater length below).

On December 4, 2000, Bristol submitted the clarification that the FDA had requested four days earlier. *See* Second Bristol Decl., dated Dec. 4, 2000 (FDA Opp'n, Ex. I). In its clarification, Bristol declared that the sole claim of the '365 patent was:

> a method for ameliorating an undesirable anxiety state comprising the direct administration of 6-hydrox-busprione [the metabolite] or oral administration of a

> prodrug[8] [buspirone] of 6-hydrox-busprione such as buspirone hydrochloride to provide an effective but non-toxic anxiolytic dose of 6-hydrox-busprione.

Id. Bristol also explained that the Bristol press release that Mylan and Danbury had provided to the FDA was "a short-hand, layperson's description of the patent." *See* Bristol Opp'n at 15. Finally, in a letter accompanying the declaration, Bristol reiterated that "the '365 patent does not simply claim a method of using [the metabolite], but also claims a method of using [buspirone itself]." *Id*. (Dec. 4, 2000 Letter) at 2.

Based on Bristol's clarification, and "consistent with [the FDA's] long-standing policy of accepting at face value the accuracy of such patent declarations, [the] FDA concluded that the Federal Circuit's ruling in *Hoechst-Roussel* was inapplicable because the '365 patent did not solely claim a metabolite." FDA Opp'n at 13. For this reason, the FDA informed Bristol that the clarification had "adequately responded" to the agency's concerns, and that the '365 patent would therefore be deemed to have been listed in the Orange Book on November 21, 2000. *See id*. (citing FDA Letter to Bristol dated Dec. 6, 2000, Ex. J).

IV. THE MARYLAND LITIGATION

On November 30, 2000, the very day that Mylan instituted litigation in this court, two other generic drug companies, Watson Pharmaceuticals and Danbury Pharmacal (hereinafter

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[8] A prodrug is a drug that converts *in vivo* to a patented form of drug, *see Zenith Labs., Inc. v. Bristol-Myers Squibb, Co.*, 1992 WL 171910, *25 (D.N.J. 1992), or as Mylan explains, "it is a drug which is metabolized into the metabolite," *see* Pl.'s Reply at 11 n.9. Thus, buspirone is a prodrug of BMY 28674. *See id*.

"Danbury")[9] filed suit in the U.S. District Court for the District of Maryland. Like Mylan, Danbury sought an injunction ordering the de-listing of Bristol's '365 patent from the Orange Book. On January 18, 2001, U.S. District Judge Frederic N. Smalkin issued a Memorandum Opinion denying the plaintiffs' request for preliminary injunctive relief. *See Watson Pharm., Inc. and Danbury Pharmacal, Inc. v. Henney*, Civil Action No. 00-3516, (D. Md. Jan. 17, 2001). In his Opinion, Judge Smalkin described Danbury's suit as, "at base, a quest for judicial review of a federal agency's final decision" under the Administrative Procedure Act ("APA"), 5 U.S.C. § 706. *See id*. at 4. It is, of course, well-established that agency determinations are entitled to deference under *Chevron U.S.A., Inc. v. Natural Resources Defense Council*, 467 U.S. 837 (1984). Noting that the FDA plays a limited, "ministerial" role in the patent fights between patent holders and generic makers, and in light of the traditional deference accorded to agency determinations, Judge Smalkin ruled that it was "not the business of the FDA or of this Court in an APA review, to adjudicate the *merits* of the scope and/or validity of the claims covered by the '365 patent." *See id*. at 5 (emphasis in original). Accordingly, Judge Smalkin ruled that since the FDA's action was not "unreasonable, arbitrary, or capricious," the federal defendants were entitled to summary judgment on the merits. *See id*.

Because Bristol and the FDA have urged this court to adopt Judge Smalkin's reasoning, it is worth examining how this case differs from the Maryland litigation. First, Danbury did not sue Bristol. *See id*. at 7. In fact, although Bristol ultimately intervened as a defendant in the Maryland

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[9] Danbury Pharmacal, Inc. is a wholly owned subsidiary of Schein Pharmaceutical, Inc., which, in turn, is a wholly owned subsidiary of Watson Pharmaceuticals, Inc. *See Watson v. Henney*, Civil Action No. 00-3516 (D. Md.) (FNS), Compl. ¶ 6.

litigation, Danbury did not request any relief against Bristol. *See id.* Second, Danbury did not raise the issue of whether Bristol's '365 patent was one as to which a claim of patent infringement could reasonably be asserted. *See id.* Finally, Danbury did not submit a Section viii Statement to the FDA, and therefore did not argue, as did Mylan, that the FDA was required to accept its Section viii Statement. *See id*.

The FDA has endorsed Judge Smalkin's ruling, reiterating to this court that its role in listing patents is "purely ministerial" and that it "does not have the expertise nor the resources to resolve complex patent coverage issues." *See* FDA Opp'n at 19 (citing 54 Fed. Reg. 28872, 28909-10 (July 10, 1989)). For this reason, among others, the FDA argues that Mylan's remedy is not to sue the agency, but rather to ask the court hearing its patent claims to modify the presumptive 30-month statutory stay on FDA approval of Mylan's ANDA. *See* FDA Opp'n at 23; *see also* 21 U.S.C. § 355(j)(5)(B)(iii) (providing that 30-month stay may be modified by the court hearing the patent litigation).

Mylan responds that it is not asking the FDA to perform anything *but* a ministerial act. As Mylan explained at oral argument, the FDA is "an important player here because if we were to sue Bristol alone and not the FDA and there were to be an order directed to Bristol asking Bristol to request [that] the patent be delisted from the Orange Book, we might still need relief against the FDA if the FDA, for whatever reason, declined to do so." *See* Tr. of Oral Argument dated Jan. 24, 2001 ("Tr.") at 8. In other words, Mylan has placed the "substantive burden" in this matter on Bristol. *See id*. at 7. Indeed, with the exception of the Section-vii-Statement issue, Mylan is challenging only Bristol's actions, not the FDA's. *See* Pl.'s Reply Mem. In Support of Mot. for Prelim. Inj. ("Pl.'s Reply") at 3-4. Specifically, Mylan asks the court to declare that *Bristol*

improperly submitted the '365 patent to the FDA for inclusion in the Orange Book. *See id.* at 4. In this way, Mylan has cleverly avoided the problem that Danbury faced in its suit, namely that the FDA's decision to list the '365 patent was entitled to a presumption of validity under *Chevron* and its progeny.

V. DISCUSSION

A. Subject-Matter Jurisdiction

Before proceeding to the preliminary-injunction analysis, the court must address Bristol's argument that Mylan does not identify any recognized cause of action in support of its request for relief. *See* Bristol Opp'n at 22-23. According to Bristol, Mylan's lawsuit is not the appropriate vehicle for challenging Bristol's submission of the '365 patent for inclusion in the Orange Book. *See id.* This is so, Bristol argues, because Mylan seeks to enforce the FFDCA—a statute which by its terms does not allow for a private right of action. *See id*. at 22; *see also* 21 U.S.C. § 337(a) ("proceedings for the enforcement, or to restrain violations, of the [statute] shall be by and in the name of the United States"). Indeed, as Bristol points out, "every federal court that has addressed the issue has held that the FFDCA does not create a private right of action." *See* Bristol Opp'n at 22 (citing *Eli Lilly & Co. v. Roussel Corp.*, 23 F. Supp.2d 460, 476 (D.N.J. 1998)); *see also In re Orthopedic Bone Screw Prods. Liab. Litig.*, 193 F.3d 781, 788 (3d Cir. 1999); *PDK Labs., Inc. v. Friedlander*, 103 F.3d 1105, 1113 (2d Cir. 1997); *Bailey v. Johnson*, 48 F.3d 965, 966-68 (6th Cir. 1995); *Mylan Labs., Inc. v. Matkari*, 7 F.3d 1130, 1139 (4th Cir. 1993), *cert. denied*, 510 U.S. 1097 (1994); *Rodriguez v. SK & F Co.*, 833 F.2d

8, 9 (1st Cir. 1987) (per curiam). For this reason, Bristol urges the court to hold that Mylan has failed to state a claim upon which relief can be granted. *See* Bristol Opp'n at 22.

Mylan, however, does not seek to enforce the FFDCA against Bristol. *See* Pl.'s Reply at 4. Rather, Mylan asks the court to declare that Bristol improperly submitted the '365 patent to the FDA for inclusion in the Orange Book because that patent did not meet 21 U.S.C. § 355(c)(2)'s requirements for such a listing. *See id*. Mylan also asks that the court, upon making this determination, order Bristol to withdraw its submission of the '365 patent, and instruct the FDA to perform the "ministerial" task of de-listing the '365 patent from the Orange Book. *See id*. Mylan contends—and the court agrees—that these requests are proper under the Declaratory Judgment Act, 28 U.S.C. § 2201. *See id*. at 4-5.

1. The Declaratory Judgment Act

The Declaratory Judgment Act permits federal courts to "declare the rights and other legal relations" of parties to "a case or actual controversy." *See* 28 U.S.C. § 2201. The Act does not enlarge the jurisdiction of federal courts beyond what is constitutionally permissible, but widens the range of remedies that federal courts have at their disposal. *See Skelly Oil Co. v. Phillips Petroleum Co*., 339 U.S. 667, 771-72 (1950). The sole requirement for jurisdiction under the Act is that the conflict be "real and immediate, *i.e.*, that there be a true, actual 'controversy.'" *See Arrowhead Indus. Water, Inc. v. Ecolochem, Inc.*, 846 F.2d 731, 735 (Fed. Cir. 1988). The "actual controversy" requirement, in turn, mirrors the "case or controversy" requirement of Article III of the United States Constitution. *See Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 239-

41 (1937). Thus, the Declaratory Judgment Act requires no more rigorous a showing of justiciability than the Constitution does.[10]

Several courts have held that an action to delist a patent from the Orange Book may be brought under the Declaratory Judgment Act. For example, in *Ben Venue Laboratories v. Novartis Pharmaceutical Corp.*, 10 F. Supp.2d 446, 451-52 (D.N.J. 1998), the defendant was the pioneer maker of Aredia, a drug designed to treat bone loss and complications from cancer. *See id*. at 450. In the Orange Book, Aredia was listed with U.S. Patent No. 4,711,880 ("the '880 patent"). *See id*. Ben Venue, a generic maker, had filed an ANDA to manufacture and sell a generic version of Aredia. Before addressing the merits of the parties' claims, the court determined that the plaintiff was entitled to request declaratory relief against an Orange-Book

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[10] Declaratory relief is "indisputably appropriate" in patent cases. *Societe de Conditionnement en Aluminium v. Hunter Eng'g Co., Inc.*, 655 F.2d 938, 943 (9th Cir. 1981) (citing *Hanes Corp. v. Millard*, 531 F.2d 585, 592 (D.C. Cir. 1972)). As the Second Circuit has explained:

> the availability of declaratory relief has destroyed the "racket" by which patentees gained manifold advantages by the device of threatening alleged infringers or their customers with lawsuits which might never be brought or, if brought, could always be dismissed without prejudice, without the possibility of such persons taking steps to ascertain the validity of the patentee's claims…. Because of the public policy in breaking this "racket," and in preventing an invalid patent from remaining in the art "as a scarecrow"… the declaratory remedy should be construed with liberality in the patent field as in general.

Wembley, Inc. v. Superba Cravats, Inc., 315 F.2d 87, 89 (2d Cir. 1963) (internal citations omitted). Thus, the Declaratory Judgment Act serves the policies underlying patent law by allowing litigants to test the validity and infringement of patents that are being used as what Judge Learned Hand called "scarecrows." *See Arrowhead*, 846 F.2d at 735 n. 4 (citing *Bresnick v. United States Vitamin Corp*., 139 F.2d 239, 242 (2d Cir. 1943)).

listing, even during the 45-day moratorium on declaratory judgments for infringement. *See id.* Indeed, the court expressly held that while a challenge to the appropriateness of an Orange Book listing may be raised as a counterclaim in a patent infringement suit, this "is not the only way such a challenge can be brought. The Court sees no reason why a party must wait until it is sued for patent infringement to raise the issue of an improper Orange Book listing." *See id*. at 452 n. 4.[11]

Bristol attempts to distinguish *Ben Venue* on the grounds that in that case, the patent holder had asserted a claim for infringement, whereas in the instant matter, there is neither a claim of patent infringement nor a claim for a declaration of non-infringement, invalidity, or unenforceability. *See* Bristol Supp. Brief at 2 n.2. Bristol fails to note, however, that Ben Venue did not bring a declaratory action for non-infringement but "only raised the propriety of the listing of the [defendant's patent] under the food and drug laws." *See Ben Venue Labs*., 10 F. Supp.2d at 451. As the court explained: "Ben Venue's lawsuit did not explicitly challenge the validity of the patent or state that its product was noninfringing. Instead, Ben Venue asserted that the '880 Patent does not 'claim' Aredia and that the patent is therefore improperly listed in the Orange Book." *Id*. at 450.

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[11] The FDA argues that the Hatch-Waxman Act "provides that interested generic and innovator firms [must] resolve any patent disputes concerning a drug, including whether a patent 'claims' the approved drug product, in private litigation." FDA Opp'n at 18 (citing 21 U.S.C. § 355(j)(2)(A)(vii)(IV); § 255(j)(2)(B); and § 255(j)(5)(B)(iii)). In *Ben Venue*, however, the court held that declaratory judgment suits brought by potential generic competitors concerning allegedly inappropriate "Orange Book" listings can be initiated outside the context of the Hatch-Waxman Act. *See Ben Venue Labs*., 10 F. Supp.2d at 451-52; *see also* Gregory J. Glover, *Regulatory Concerns & Market Exclusivity*, 1175 PLI/CORP 629, 646 (2000) (stating that if "other courts" adopt the view of the *Ben Venue* court, generic competitors will be able to raise Orange Book listings substantially in advance of having to make patent certifications in generic applications).

Bristol also fails to note another critical factor in the *Ben Venue* decision, namely that the defendant did not file a patent infringement suit against Ben Venue until after Ben Venue had filed its declaratory judgment action. *See id.* In other words, as in the present matter, when Ben Venue brought its declaratory judgment action, the defendant had not yet filed its suit for patent infringement. *See id.* Finally, although Ben Venue later amended its pleadings to add a claim for declaratory judgment of non-infringement, the court specifically held that the original declaratory-judgment claim was not jurisdictionally barred. *See id*. at 452. For these reasons, Bristol's efforts to distinguish *Ben Venue* are unavailing.

Similarly, in *Zenith Laboratories, Inc. v. Abbott Laboratories, Inc.*, the plaintiff ANDA applicant sought a declaration that the defendant NDA-holder had improperly listed its patents in the Orange Book. *See Zenith Labs.*, 1996 U.S. Dist. LEXIS 22567, *20 (D.N.J. 1996). The defendant moved to dismiss on the same ground advanced here by Bristol—that the plaintiff's action was an attempt to enforce the FFDCA and that the FFDCA does not provide a private cause of action. The Court denied the defendant's motion, stating that it " is not an action under the FFDCA plaintiff seeks to pursue but [rather an action] under the Declaratory Judgment and All Writs Acts and state law." *See id*. at 22.[12]

Bristol again attempts to distinguish *Zenith*, arguing that unlike Mylan, the generic maker-plaintiff in *Zenith* sought a declaratory judgment of non-infringement, invalidity or unenforceability.

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[12] The *Zenith* court also noted that the Northern District of Illinois had entertained a request for a declaratory judgment against Abbott, found Abbott's listings to be improper, and ordered Abbott to remove those patents from the Orange Book. *See id.* at 22 n.2 (citing *Abbott Labs. v. Geneva Pharms.*, 1996 U.S. Dist. LEXIS 9762 (N.D. Ill. 1996)).

See Bristol Supp. Brief at 2 n.2. As Bristol states, "[w]e are not aware of a single case holding that an action to delist a patent from the Orange Book is properly grounded solely upon the [Declaratory Judgment Act] where there is neither a claim of patent infringement nor a claim for a declaration of non-infringement, invalidity or unenforceability." *Id*. Mylan responds that because there must be subject-matter jurisdiction over each claim in a lawsuit, the fact that there was also a claim for declaratory judgment of non-infringement in *Zenith* is irrelevant. *See* Pl.'s Supp. Reply Supp. Brief at 2 (citing *Mineba Co., Ltd. v. Papst*, 13 F. Supp.2d 35, 40 (D.D.C. 1998) (dismissing certain counts for lack of subject-matter jurisdiction while declining to dismiss other declaratory-judgment counts that "arise under" the patent laws)).

Bristol's efforts to distinguish *Zenith* and *Ben Venue* take aim at a more fundamental issue: whether there is an underlying basis for federal jurisdiction here beyond the Declaratory Judgment Act. As Bristol correctly noted at oral argument, the Declaratory Judgment Act, standing alone, does not confer jurisdiction on a federal court. *See* Tr. at 28; *see also Skelly Oil Co. v. Phillips Petroleum Co.*, 339 U.S. 876, 878-79 (1950) (the "operation of the Declaratory Judgment Act is procedural only"); *Superlease Rent-A-Car, Inc. v. Budget Rent-A-Car of Md., Inc*., 1989 WL 39393, *3 (D.D.C. 1989) (holding that because Declaratory Judgment Act provides no independent cause of action, the plaintiff must first assert an interest in itself which the law recognizes). Thus, independent of the applicability of cases like *Zenith* and *Ben Venue*, the court must determine whether it has subject-matter jurisdiction over Mylan's request for declaratory judgment.

The test for determining whether an actual controversy exists in a patent case has been phrased in many ways, depending on the facts of the particular case. *See Mineba Co., Ltd. v.*

Papst, 13 F. Supp.2d at 39. In the classic patent declaratory judgment suit, the two core elements of the test are: (1) whether the defendant's acts create a "reasonable apprehension" on the part of the plaintiff that it will face an infringement suit or whether "the acts of the defendant indicate an intent to enforce its patent;" and (2) whether acts of the plaintiff might subject it or its customers to a suit for patent infringement. *See id.* (citations omitted); *see also DuPont Merck Pharm. Co. v. Bristol-Myers Squibb*, 62 F.3d 1397, 1401 (Fed. Cir. 1995).[13] Notably, there need not be an express threat of infringement to establish an actual case or controversy. *See Goodyear Tire & Rubber Co. v. Releaseomers, Inc.*, 824 F.2d 953, 955-56 (Fed. Cir. 1987). As the Federal Circuit has held, such a requirement would defeat the purpose of the Declaratory Judgment Act, which in patent cases is to provide the allegedly infringing party relief from uncertainty and delay regarding its legal rights. *See id.* (citing Moore's Federal Practice ¶ 57.08[2] (1986)).

Mylan satisfies both elements of the test. First, Bristol's actions have created a reasonable apprehension in Mylan that it could face an infringement suit or that Bristol intends to enforce its patent. By listing the '365 patent in the Orange Book, Bristol represented that the patent satisfies the requirements of 21 U.S.C. § 355(c)(2). In other words, Bristol represented that the '365 patent is one "with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use or sale" of buspirone and that

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[13] Satisfaction of this two-part test is not a prerequisite to jurisdiction in every possible patent declaratory-judgment action. *See Fina Oil & Chem. Co. v. Ewen*, 123 F.3d 1466, 1470 (Fed. Cir. 1997). "Indeed, the two elements merely assure that the declaratory plaintiff has enough interest in the subject matter of the suit and that the disagreement between the parties is real and immediate enough to fulfill the 'actual controversy' requirement. *See id*.

the '365 patent "claims a method of using" buspirone. *See* 21 U.S.C. § 355(c)(2); Decl. of Richard P. Ryan (FDA Opp'n , Ex. I). Moreover, in its Petition to Expedite Issuance of [the '365] Patent, Bristol represented to the PTO that "to maintain its product position in what becomes a highly competitive market, assignee requires issuance of this patent *prior to November 22, 2000*." Mot. for Prelim. Inj., Leff Decl., Ex. 1 at M156 (emphasis in original). The purpose of this representation (as characterized by Mylan) was to ensure that the '365 patent could be listed in the Orange Book before the expiration of Bristol's pediatric exclusivity and to permit Bristol to use the Hatch-Waxman Act's certification and lawsuit-filing procedures to block FDA approval of Mylan's ANDA. *See* Pl.'s Supp. Brief at 4. Finally, on November 27, 2000, Bristol's Senior Patent Counsel sent a letter to Mylan specifically calling attention to the '365 patent and giving Mylan directions on how to serve a Paragraph IV notice on Bristol with respect to that patent. *See id*., Ex. B. Bristol's actions indicate that Mylan was in reasonable apprehension of being sued and that, by causing the '365 patent to be listed in the Orange Book, Bristol effectively blocked FDA approval of Mylan's ANDA. *See* Pl.'s Supp. Brief at 4.

With respect to the second requirement for a patent controversy, the Federal Circuit has held that a plaintiff "must be engaged in an actual making, selling, or using activity subject to an infringement charge or must have made meaningful preparation for such activity." *See Arrowhead*, 846 F.2d at 736. Mylan is in a position to begin marketing its generic product immediately upon FDA approval. Indeed, Mylan has already developed a generic equivalent of BuSpar®, filed an ANDA with respect to that product, obtained tentative FDA approval of its ANDA, and packed its buspirone product into trucks and onto the loading dock on November 21, 2000 in anticipation of final FDA approval. *See* Pl.'s Response at 4. Thus, not only did Mylan engage in potentially

infringing activity, it was only twelve hours away from selling its product. *See id.* By contrast, courts have held that the more acute case-or-controversy problem arises when the plaintiff has not yet begun to manufacture, or make preparations to manufacture, the patented product. *See, e.g.*, *Societe de Conditionnement en Aluminium v. Hunter Eng'g Co., Inc.*, 655 F.2d 938, 944 (9th Cir. 1981). "In that situation, the plaintiff is asking the court to render an advisory opinion whether its product would be infringing a valid patent." *See id*. Mylan's substantial preparations for the sale of its generic buspirone product demonstrate that it does not seek an advisory opinion.

2. Is This a "Patent Case"?

Notwithstanding the above discussion, Bristol argues that this two-part test does not apply because the instant matter is not a "patent case." *See* Bristol Supp. Brief at 2, 2 n.1. Indeed, Bristol argues that Mylan has simply fashioned this case as a "patent case" in an effort "to create the appearance of a justiciable case or controversy," when in fact "[t]his is an administrative law case in which Mylan challenges [Bristol's] submission to the FDA of information relating to the '365 patent and the FDA's decision to publish BMS's submission in the Orange Book and to withhold approval of Mylan's ANDA prior to the expiration of the waiting period imposed by Congress." *See* Bristol Supp. Brief at 3.

Bristol's contention that this is not a "patent case" implicitly challenges whether Mylan's case "arises under" the federal patent laws. Under 28 U.S.C. § 1338(a), "district courts shall have original jurisdiction of any civil action arising under any Act of Congress relating to patents…." In *Christianson v. Colt Indus. Operating Co.*, 486 U.S. 800, 808-809 (1988), the Supreme Court outlined the dimensions of section 1338(a):

> [Section] 1338(a) jurisdiction likewise extend[s] only to those cases in which a well-pleaded complaint establishes either that federal patent law creates the cause of action or that the plaintiff's right to relief necessarily depends on resolution of a substantial question of federal patent law, in that patent law is a necessary element of one of the well-pleaded claims.

Id. Thus, section 1338(a) gives district courts jurisdiction over causes of action created by federal law *and* causes of action whose resolution depends on a substantial question of federal patent law. *See id.*; *Additive Controls & Measurement Sys., Inc. v. Flowdata, Inc.*, 986 F.2d 476, 478 (Fed. Cir. 1993). The Federal Circuit recently stated that *Christianson* sets a "lenient standard" for jurisdiction under 28 U.S.C. § 1338(a). *See United States Valves, Inc. v. Dray*, 212 F.3d 1368, 1372 (Fed. Cir. 2000).

A purported declaratory judgment action must be analyzed pursuant to the well-pleaded complaint rule. *See, e.g., Speedco, Inc. v. Estes*, 853 F.2d 909, 912 (Fed. Cir. 1988). The well-pleaded complaint rule is applied "not to the declaratory judgment complaint, but to the action that the declaratory defendant would have brought." *Minebea Co. v. Papst*, 13 F. Supp.2d 35, 40 (D.D.C. 1998) (citations omitted). Here, the action that Bristol—the declaratory defendant—would have brought was a claim for infringement of the '365 patent. It would not have been, as Bristol contends, a suit by Bristol against Mylan to require listing of the '365 patent in the Orange Book. *See* Bristol Supp. Brief at 2. Because a claim for patent infringement "is clearly a claim which 'arises under' the patent laws as contemplated by 28 U.S.C. § 1388(a)," the court has subject-matter jurisdiction over Mylan's claims against Bristol. *See Mineba*, 13 F. Supp.2d at 40; *see also* Mylan Supp. Reply Brief at 4-5 ("It would be hard to imagine an issue which depends more on a substantial question of federal patent law than whether the '365 patent

covers … BuSpar® and whether a claim for patent infringement could reasonably be asserted against that product").

Finding jurisdiction in this case is not inconsistent with *Speedco, Inc. v. Estes*, 853 F.2d 909 (Fed. Cir. 1988). In that case, the court held that the declaratory defendant's hypothetical action would not "arise under" the federal patent law because the defendant did not have a colorable claim of ownership in the subject patent and therefore had no right to sue for patent infringement. *See id.* The declaratory defendant's only other possible claim was for breach of contract relating to a patent, which would not have required the declaratory defendant to plead patent validity as a necessary element of the complaint. *See id*. The court thus concluded that the declaratory plaintiff could not establish jurisdiction under the well-pleaded complaint rule. *See id*. By contrast, the action Bristol would have brought here was a claim for infringement of the '365 patent—clearly an action "arising under" the patent laws for the purpose of federal jurisdiction.

Based on this analysis, the court concludes that Mylan has stated a recognized cause of action in support of its request for relief, and that this court has subject-matter jurisdiction to hear this cause of action. In addition, Mylan has demonstrated that this matter does present a case or controversy such that this court is not in the position of rendering an advisory opinion. *See, e.g.*, *Flast v. Cohen*, 392 U.S. 83, 96-97 (1968) (discussing origins of prohibition on advisory opinions). Accordingly, the court will proceed to the preliminary-injunction analysis.

C. Preliminary Injunction Standard

A preliminary injunction is an extraordinary form of judicial relief. *See Moore v. Summers*, 113 F. Supp.2d 5, 17 (D.D.C. 2000). Although the issuance or denial of a preliminary

injunction rests in the sound discretion of the trial court, it is not a form of relief granted lightly. *See Ambach v. Bell*, 686 F.2d 974, 979 (D.C. Cir. 1982). Traditionally, courts must examine four factors: (1) whether there is a substantial likelihood that the plaintiff will succeed on the merits; (2) whether the plaintiff will be irreparably injured if an injunction is not granted; (3) whether an injunction will substantially injure the non-moving party; and (4) whether the public interest will be furthered by the injunction. *See* Fed. R. Civ. P. 65; *Serono Labs. v. Shalala*, 158 F.3d 1313, 1317-18 (D.C. Cir. 1998); *Washington Metro. Area Transit Comm'n v. Holiday Tours, Inc.*, 559 F.2d 841, 843 (D.C. Cir. 1977). Courts do not consider these factors in isolation from one another, and no one factor is necessarily dispositive. *See CityFed Fin. Corp. v. Office of Thrift Supervision*, 58 F.3d 738, 746 (D.C. Cir. 1995). Rather, the factors "interrelate on a sliding scale and must be balanced against each other." *Davenport v. Int'l Bhd. of Teamsters*, 166 F.3d 356, 361 (D.C. Cir. 1999) (citing *Serono Labs.*, 158 F.3d at 1317-18).

If the plaintiff makes a particularly weak showing on one factor, however, the other factors may not be enough to compensate. *See Taylor v. Resolution Trust Corp.*, 56 F.3d 1497, 1506 (D.C. Cir. 1995), *amended on other grounds on reh'g*, 66 F.3d 1226 (D.C. Cir. 1995). Indeed, in this Circuit, the first factor—likelihood of success on the merits—is the most important one, for absent such an indication, "it would take a very strong showing with respect to the other preliminary injunction factors to turn the tide in plaintiffs' favor." *See Davenport*, 166 F.3d at 366 (citing *Murrow Furniture Galleries v. Thomasville Furniture Indus.*, 889 F.2d 524, 527 (4th Cir. 1989)).

In this case, Mylan faces an additional hurdle because it seeks a mandatory injunction as opposed to a prohibitive injunction. *See Mylan Pharms., Inc. v. Shalala*, 81 F. Supp.2d 30, 36

(D.D.C. 2000); *Mylan Pharms, Inc. v. Henney*, 94 F. Supp.2d 36, 58 (D.D.C. 2000) (Urbina, J.). That is, Mylan seeks a preliminary injunction not to maintain the status quo while this matter can be resolved on the merits, but rather to alter the status quo by requiring the FDA to approve its ANDA. In this Circuit, "the power to issue a preliminary injunction, especially a mandatory one, should be sparingly exercised." *See Mylan*, 94 F. Supp.2d at 58 (citing *Dorfmann v. Boozer*, 414 F.2d 1168, 1173 (D.C. Cir. 1969) (internal quotations and citations omitted)); *see also Columbia Hosp. for Women Found., Inc. v. Bank of Tokyo-Mitsubishi, Inc.*, 15 F. Supp.2d 1, 4 (D.D.C. 1997), *aff'd*, 159 F.3d 636 (D.C. Cir. 1998).

D. Preliminary-Injunction Analysis

1. Prong 1: Whether Mylan is Likely to Succeed on the Merits

Under the first prong of the preliminary-injunction analysis, the court must consider whether the movant is likely to succeed on the merits. Mylan states that it is entitled to immediate FDA approval of its ANDA, and therefore is likely to succeed on the merits, for two "separate and independently sufficient" reasons. *See* Mot. for Prelim. Inj. at 3. First, Mylan argues that the '365 patent does not meet the two statutory listing requirements of 21 U.S.C. §§ 355(b)(1) and (c)(2). *See id.* Second, Mylan argues that "even if the '365 patent were properly listed, the FDA violated the applicable statute and its long-standing practice by refusing to accept Mylan's [Section viii Statement] that the '365 patent 'does not claim a use for which [Mylan] is seeking approval.'" *Id*. Because the court finds Mylan's Section-viii-Statement argument unpersuasive,[14] the court will

[14] In brief, Mylan's Section-viii-Statement argument is as follows: Bristol submitted a statement to the FDA to the effect that the '365 patent covers all approved uses for BuSpar®. Mylan submitted a Section viii Statement to the FDA certifying that its labeling

focus primarily on Mylan's contention that Bristol's '365 patent does not meet the two statutory listing requirements of 21 U.S.C. §§ 355 (b)(1) and (c)(2).

Mylan argues that the '365 patent has been improperly listed because: (1) the patent does not meet the statutory listing requirement that it "claim the drug" or "a method of using" the drug for which Bristol had obtained FDA approval; and (2) the patent does not meet the statutory requirement that "a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the [approved] drug." *See* Mot. for Prelim. Inj. at 3 (citing 21 U.S.C. § 355(b)(1)).

With respect to the first of these listing requirements, Mylan argues that the '365 patent claims a method of using a buspirone metabolite (BMY 28674). *See id.* The patent does not, contends Mylan, claim buspirone—the approved drug—or a method of using buspirone. *See id*. As for the second listing requirement, Mylan contends that Bristol's representation that a claim of patent infringement could reasonably be asserted against an unauthorized user, maker or seller of

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did not claim a method of use covered by the '365 patent. Mylan argues that the FDA was required to accept its Section viii Statement, which was required and authorized by statute, and reject Bristol's statement, which was not required by statute, and therefore was "gratuitous." *See* Mot. for Prelim. Inj. at 28. In other words, Mylan argues that the FDA should defer to its interpretation of the scope of the '365 patent and not to Bristol's submission identifying the protected use.

For the purposes of the present motion, the court does not find it necessary to engage in a lengthy discussion of Mylan's Section-viii-Statement argument, particularly since Mylan has demonstrated a substantial likelihood of success on the merits of its other two arguments. The court does note, however, that Bristol has offered a persuasive characterization of Mylan's argument: "In effect, Mylan argues that it is the final arbiter of whether or not a method of use patent covers the use for which it is seeking approval, and that the FDA was bound to accept Mylan's judgment on that question." Bristol Opp'n at 20.

the approved drug was false because "the '365 patent makes quite plain, by its express language, that to the extent that the 'systemic administration' of BMY 28674 can be accomplished by administration of buspirone itself, the claimed invention includes administration of buspirone only 'in such a manner that the metabolic production of BMY 28674 is favored.'" *See id*. at 6 (citing '365 patent, col. 12, lines 14-15, Leff Decl. Ex. 3).

The court will address in turn the two statutory listing requirements of 21 U.S.C. § 355(c) and Mylan's arguments with respect to each.

a. The '365 Patent Does Not "Claim" a Method of Using BuSpar®

With respect to the first statutory listing requirement—that the '365 patent claim a method of using the approved drug—Mylan relies on Federal Circuit precedent to suggest that the '365 patent does not claim a method of using BuSpar®. Specifically, Mylan argues that Bristol's filing of the '365 patent violated the Federal Circuit's holding in *Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997) ("*Hoechst*"). Because *Hoechst* dealt with a different provision of the Hatch-Waxman Act than the provision at issue here, the court must first determine whether *Hoechst* is applicable to the case at bar.

In *Hoechst*, the Federal Circuit considered whether a drug manufacturer could obtain a patent term extension under 35 U.S.C. § 156 of the Hatch-Waxman Act ("Section 156"). Section 156 provides that:

> (a) the term of a patent *which claims a product, a method of using a product*, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent if…

* * *

> (4) the product has been subject to a regulatory review period before its commercial marketing or use.

35 U.S.C. § 156(a) (emphasis added). Bristol submitted the '365 patent to the FDA for listing in the Orange Book pursuant to 21 U.S.C. § 355(c)(2) ("Section 355"). Section 355 requires, among other things, that the patent "claim a method of using" the approved drug. *See* 21 U.S.C. §§ 355(c)(2). Mylan argues that because Section 156 and Section 355 both require that a patent "claim a method" of use, the Federal Circuit's holding in *Hoechst* should apply to the instant matter.

A summary of the *Hoechst* decision may help frame the issues that Mylan has raised. In 1990, Warner-Lambert Co. ("Warner") submitted an NDA to the FDA for approval of COGNEX® to treat Alzheimer's disease. *See Hoechst*, 109 F.3d at 757. The active ingredient in COGNEX was tacrine hydrochloride. *See id.* In 1993, the FDA granted Warner approval to market COGNEX®, whereupon Hoechst sued Warner for infringement of Hoechst's '286 patent, which had issued in 1986. *See id*. Hoechst's '286 patent did not claim tacrine hydrochloride itself; rather, it disclosed and claimed both the compound 1-hydroxy-tacrine and a method of treating patients in need of memory enhancement by administering an effective amount of 1-hydrox-tacrine. *See id*. In addition, and of moment to Mylan's claim, tacrine hydrochloride metabolized into 1-hydroxy-tacrine and other compounds after ingestion. *See id*.

While in litigation over the alleged infringement of the '286 patent, Hoechst applied for an extension of the term of its patent pursuant to Section 156, based on the Warner-initiated regulatory review period of COGNEX®. *See id.* Hoechst argued that it was entitled to this

extension because the administration of the approved drug product resulted in the production in the body of the metabolite, and that administration of the drug product itself therefore infringed the patent claim. In 1995, the Commissioner of Patents and Trademarks denied Hoechst's application for an extension. The Commissioner decided that, among other things, Hoechst's '286 patent did not "claim" either tacrine hydrochloride or a method of using that product. *See id*. at 758.

On appeal to the Federal Circuit, Hoechst argued that a patent "claims" an FDA-approved product within the meaning of Section 156 if the FDA-approved product would infringe a claim of that patent. *See Hoechst*, 109 F.3d at 758. Because use of tacrine hydrochloride allegedly infringed its claim to a method of using 1-hydroxy-tacrine, Hoechst argued that the '286 patent "claimed" a method of using tacrine hydrochloride. *See id.* The Federal Circuit sided with the Commissioner, holding that Hoechst's '286 patent claimed neither tacrine hydrochloride nor a method of using that product. *See id*. at 761. Mylan argues here that just as the metabolite patent in *Hoechst* did not "claim" the drug product or the method of its use, so too Bristol's '365 patent does not "claim" a method of using BuSpar®. *See* Mot. for Prelim. Inj. at 18. According to Mylan, *Hoechst* demonstrates that the '365 patent is not properly listed in the Orange Book because it *claims* neither the approved drug nor a method of administering it. *See id*.

Bristol responds that Mylan's reliance on the *Hoechst* case is misplaced because *Hoechst* involved a different statute (Section 156) and thus a different issue (whether a drug manufacturer could obtain a patent term under section 156). *See* Bristol Opp'n at 26. In fact, Section 355 and Section 156 are, in a sense, competing provisions of the same act. Section 156 (which Judge Smalkin described as the "carrot" portion of the Hatch-Waxman Act) provides patent holders with an increased incentive for drug research and innovation by restoring some of the time lost in

regulatory review to their patent term. *See* H.R. Rep. No. 98-857, pt. I at 15 (1984). Section 355 relates to the expedited approval for generic equivalents (and forms part of what Judge Smalkin described as the "stick" portion of the Act).

In *Hoechst*, the primary issue facing the Court was the meaning of the statutory term "claims." *See Hoechst*, 109 F.3d at 758. Noting that statutory words must be given their ordinary meaning unless "otherwise defined" by Congress, the *Hoechst* Court found nothing in the legislative history of Section 156 to suggest that Congress had "otherwise defined" the word "claims." *See id*. at 759-60. Quite to the contrary, the court read the legislative history of Section 156 to suggest that Congress had "deliberately chosen the term 'claims' because [the word] already had a well-known meaning and usage in patent law. *See id*. at 760. Based on its interpretation of the term "claims," the Federal Circuit concluded that there was a difference between claiming the chemically distinct product and the method of using the product, and claiming the active ingredient that has received FDA approval, or a method of using that ingredient.

Although Section 156 implements different policies than Section 355, this court has not found, and Bristol has not cited, anything from the legislative history of the Hatch-Waxman Act to suggest that the plain language of Section 156 and the plain language of Section 355 should be interpreted differently. Nor has Bristol suggested that the word "claims," as used in Section 355, is ambiguous. It is a well-known maxim of statutory interpretation that when "the terms of a statute [are] unambiguous, judicial inquiry is complete, except in rare and exceptional circumstances." *See Rubin v. United States*, 449 U.S. 424, 430 (1981). Thus, in the absence of any "exceptional circumstances," ambiguities, or indications to the contrary, the court determines that the Federal Circuit's interpretation of the word "claims" in Section 156—an interpretation based entirely on

plain meaning—is compelling authority in this court's interpretation of Section 355. *Hoechst* suggests that Bristol's '365 patent claims neither the approved drug (BuSpar®) nor a method of administering it.

In response to this *Hoechst*-based argument, Bristol argues that, unlike the patent at issue in *Hoechst*, its '365 patent is not limited to the use of a metabolite. *See* Bristol Opp'n at 26. Rather, Bristol states that the '365 patent "encompasses a method of use of BuSpar®--*i.e.*, the 'oral administration of a precursor or product form of … buspirone.'" *Id*. (citing '365 patent, Col. 12, lines 3-5). As Mylan correctly points out, however, the prosecution history of the '365 patent shows that: (1) Bristol tried to claim the administration of buspirone as a prodrug; (b) the PTO would not allow it; and (3) Bristol surrendered that subject matter. *See* Pl.'s Reply at 15. These three facts suggest that just as the patent in *Hoechst* was limited to the metabolite, so too is the '365 patent limited to the use of the metabolite BMY 28674, and therefore the '365 patent cannot claim the administration of buspirone.

Nevertheless, to determine whether Mylan's arguments indicate a substantial likelihood of success on the merits, the court must undertake a preliminary construction of the '365 patent claim. The court must also determine whether the filing of the '365 patent met the second statutory listing requirement of the Hatch-Waxman Act—that is, whether a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of BuSpar®.

b. The '365 Patent is Not One "With Respect to Which a Claim of Patent Infringement Could Reasonably be Asserted"

A statutory prerequisite to Orange Book listing is that "a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the [approved] drug." *See* 21 U.S.C. § 355(c)(2). For the purposes of a preliminary injunction, Mylan makes two arguments that suggest that Bristol cannot satisfy this statutory prerequisite. First, Mylan argues that during the prosecution of the '365 patent prosecution, Bristol expressly surrendered the subject matter it now contends is covered by the claim of the '365 patent—the administration of buspirone. *See* Mot. for Prelim. Inj. at 7 n.4, 25-27. Second, Mylan argues that even assuming that the claim of the '365 patent covers the administration of buspirone, it cannot cover the administration of buspirone as currently approved by the FDA. *See* Pl.'s Reply at 13.

To determine whether Mylan's arguments are correct—and whether the '365 patent is one with respect to which a claim of patent infringement could reasonably be asserted—the court must determine the proper construction of that claim.

(1) Claim Construction—The '365 Patent Expressly Disclaims Coverage of the Administration of Buspirone in the Manner Currently Approved

The construction of a patent claim is a matter of law exclusively for the court. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976-78 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996). "It is well settled that, in interpreting an asserted claim, the court should look first to the *intrinsic* evidence of record, *i.e.*, the patent itself, including the claims, the specification and, if in evidence, the prosecution history." *Vitronics Corp. v. Conceptronic, Inc.*,

90 F.3d 1576, 1582 (Fed. Cir. 1996). "Such intrinsic evidence is the most significant source of the legally operative meaning of the disputed claim language." *Id.* (internal quotation marks omitted)). By contrast, the court should look to the extrinsic evidence only if the intrinsic evidence alone fails to resolve any ambiguity in a disputed claim term.

Even within the intrinsic evidence, "there is a hierarchy of analytical tools." *See Digital Biometrics, Inc. v. Identix, Inc*., 149 F.3d 1335, 1344 (Fed. Cir. 1998). "The actual words of the claim are the controlling focus." *Id*. (citing *Thermalloy, Inc. v. Aavid Eng'g, Inc.*, 121 F.3d 691, 693 (Fed. Cir. 1997)). "The written description is considered, in particular to determine if the patentee acted as his own lexicographer, as our law permits, and ascribed a certain meaning to those claim terms. If not, an ordinary meaning, to one skilled in the art, of the claim controls." *Id*.; *see also Vitronics Corp.*, 90 F.3d at 1582 ("Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or the file history"). In construing the words of the claim, "the specification acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." *Vitronics Corp*., 90 F.3d at 1582. Indeed, the specification is considered "the single best guide to the meaning of a disputed term." *Id*.

Turning to the first tool in claim construction—the actual words—the court observes that the '365 patent contains a single claim:

> A process for ameliorating an undesirable anxiety state in a mammal comprising systemic administration to the mammal of an effective but non-toxic anxiolytic dose of [BMY 28674] or a pharmaceutically acceptable acid addition salt, prodrug, or hydrate thereof.

Mot. for Prelim. Inj. at 21 (citing '365 patent, col. 16, lines 26-32). In construing this claim, it is necessary to determine what "systemic administration of an effective but non-toxic anxiolytic dose" of BMY 28674 means.

Mylan and Bristol agree that the rules of claim construction require the court to construe the phrase "systemic administration" in view of the disclosure in the specification of the '365 patent. *See* Bristol Opp'n at 24 (citing *Vitronics Corp.*, 90 F.3d at 1582); Mot. for Prelim. Inj. at 21 (same). Here the specification states that:

> Systemic administration of BMY28674 may be accomplished by oral administration of a precursor or prodrug form of BMY28674, *e.g.*, buspirone, to mammals.

Mot. for Prelim. Inj. at 21-22 (citing '365 patent, col. 12, lines 3-8). According to Bristol, the specification teaches that there are at least two ways systemically to administer 6-hydroxy-buspirone to treat anxiety. *See* Bristol Opp'n at 24-25. The first way is direct administration of 6-hydroxy-buspirone, referred to in the patent as BMY 28674. *See id*. at 25. The second way, says Bristol, is oral administration of a prodrug such as buspirone. *See id*. Indeed, the specification itself speaks of both direct administration of BMY28674 and oral administration of a prodrug. *See id*. In light of the rules of claim construction, Bristol argues that the phrase "systemic administration" in claim 1 of the '365 patent must be construed as it is expressly defined in the patent itself, *i.e.*, as embracing direct administration *and* oral administration. Thus, Bristol concludes, unlike the patent at issue in *Hoechst*, the '365 patent is not limited to use of a metabolite. Rather, it encompasses a method of use of BuSpar®--*i.e.*, "the oral administration of a precursor or prodrug form of BMY 28674, *e.g.* buspirone." *See* Bristol Opp'n at 26 (citing '365 patent, Col. 12, lines 3-5).

To be properly filed with the FDA and listed in the Orange Book, the '365 patent must cover the same method of using BuSpar® as is currently approved.[15] The flaw in Bristol's argument is that it does not address the fact that the '365 patent expressly disclaims coverage of the administration of buspirone in the manner currently approved. For example, the specification states:

> However, this method of systemic administration of BMY28674 improves upon and *differs from the known standard method of oral administration of buspirone*.

Mot. for Prelim. Inj. at 21-22 (citing '365 patent, col. 12, lines 3-8) (emphasis added). The specification also states that the claimed invention "is in contradiction to currently-accepted methods of administration" and "is directly counter to the past method of orally administering buspirone." *See* Pl.'s Reply at 13 (citing '365 Patent, col. 12, lines 17-18, 58-59).[16]

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[15] In determining whether a claim of patent infringement can reasonably be asserted against one who manufactures, uses or sells BuSpar®, one looks only to currently approved uses of buspirone. *See* Pl.'s Reply at 13 n. 12; FDA Opp'n at 28 (the "FDA requires NDA sponsors to submit to the agency for listing only patents covering approved uses of the drug or uses for which the NDA applicant is seeking approval").

[16] During oral argument, Mylan offered the following analogy to explain why Bristol made these representations in the patent specification:

> Let's assume that a Bristol scientist had found … that a particular chemical compound in an apple was metabolized in the human body into a compound we will call "Apple-A" and that when you administer Apple-A it improve[s] health…. They file a patent application and get a patent on the systemic administration of Apple-A…. They make tablets with Apple-A. They sell those tablets. They want to stop other people from making tablets with Apple-A in them. That is fine. That is a complicated case involving issues of inherency. This is not a complicated case because what they have done here is they have tried to use this patent to stop people from selling and eating apples by arguing that when you eat an apple, it is metabolized in the human body into the equivalent of the Bristol metabolite, the equivalent of Apple-A.

Tr. at 16.

Mylan explains that these references to "currently accepted methods of administration" and "the past method of orally administering buspirone" are to the currently accepted uses of BuSpar® as reflected in the BuSpar®™ labeling—a labeling that the statute requires Mylan to use with respect to its buspirone product. *See* Mot. for Prelim. Inj. at 19. Thus, Mylan argues, according to the '365 patent itself, the use of BuSpar® in accordance with its current labeling would not infringe the '365 patent.[17] *See id*.

For this reason, Mylan interprets the specification to suggest that "the proper construction of the claim of the '365 patent does not cover the conventional mode of administering buspirone—that method set out in the approved NDA for BuSpar®." Mot. for Prelim. Inj. at 22. If Mylan is correct—and Bristol has not suggested why it would not be—the '365 patent cannot claim a method of using BuSpar® (buspirone) with respect to which a claim of patent infringement could reasonably be asserted. *See id*. (citing 21 U.S.C. § 355(b)(1)).

Indeed, in its opposition brief, Bristol provides a lengthy and persuasive discussion of why Mylan's Section-viii-Statement argument lacks merit. *See* Bristol Opp'n at 17-22. By contrast, Bristol devotes little attention to Mylan's construction of the claim of the '365 patent. *See* Bristol Opp'n at 25-27. Instead, Bristol dismisses Mylan's points as "intricate arguments of non-

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[17] In support of its argument, Mylan cites Bristol's Press Release of November 21, 2000, in which Bristol states: "with this patent protection, the company will undertake additional clinical research and development activities to elucidate the optimal use of BuSpar®, information that may be submitted for potential labeling changes." *See* Mot. for Prelim. Inj. at 19 (citing Leff Decl. Ex. 8). The court agrees with Bristol that the words of the patent itself, not the press release, define the legal scope of the '365 patent. *See* Bristol Opp'n at 25 n.9 (citing *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Accordingly, the court will not rely on Bristol's press release for guidance as to the meaning of the '365 patent claim.

infringement and invalidity" and "sophisticated efforts to construe patent claims." Bristol Opp'n at 27. According to Bristol, "all that is necessary to establish that a reasonable claim of infringement could be asserted here" is that "Mylan seeks FDA approval to market generic buspirone to treat anxiety … and the '365 patent, as discussed above, covers (among other things) the use of buspirone to treat anxiety." *Id*.

In making this argument, Bristol ignores the fact that "the scope of patent claims is as specific and concrete as the boundaries of real property." *See* Pl.'s Reply at 14; *General Foods Corp. v. Studiengesellschaft Kohle mbH,* 972 F.2d 1272, 1274 (Fed. Cir. 1992) ("The Supreme Court has likened patent claims to the description of real property in a deed 'which sets the bounds to the grant which it sanctions'") (citing *Motion Picture Patents Co. v. Universal Film Mfg. Co.*, 342 U.S. 502, 510 (1917)). As Mylan notes, "[i]t is no more sufficient to say that the patent 'covers the use of buspirone to treat anxiety' than it would be for one to say that his property is defined by the area around the old oak tree at the top of the hill." Pl.'s Reply at 2.

Bristol has not challenged Mylan's construction of the '365 patent claim. Bristol has not rebutted Mylan's arguments that if Bristol tried to extend the coverage of the '365 patent to past methods of administering buspirone, the patent would be invalid. In short, Bristol has not refuted Mylan's showing that the '365 patent is one with respect to which a claim of patent infringement could reasonably be asserted.

i. Claim Construction—Bristol Surrendered the Claim Coverage of the Administration of Buspirone During the Prosecution of the '365 Patent

Bristol's argument that the '365 patent is not limited to the use of a metabolite is unconvincing for still another reason: in the prosecution history, Bristol surrendered the subject matter it now says is covered by the claim of the '365 patent, namely, the administration of the prodrug.

The prosecution history of a patent—part of the intrinsic evidence of a patent claim's scope—contains the complete record of all the proceedings before the PTO, including any express representations made by the applicant regarding the scope of the patent claims. *See Vitronics Corp*., 90 F.3d at 1582. "As such, the record before the [PTO] is often of critical significance in determining the meaning of the claims." *Id.* Moreover, the prosecution history "limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution." *Southwall Tech., Inc. v. Cardinal IG Co*., 54 F.3d 1570, 1576 (Fed. Cir. 1995).

The Federal Circuit has repeatedly held that when a patent applicant surrenders subject matter during the prosecution of the patent, it cannot then assert a claim that encompasses the surrendered subject matter. *See, e.g., Spectrum Int'l v. Sterilite Corp.*, 164 F.3d 1372, 1379 (Fed. Cir. 1998) ("a patentee, after relinquishing subject matter to distinguish a prior art reference … 'cannot during subsequent litigation escape reliance [by the defendant] upon this unambiguous surrender of subject matter"); *Southwall Tech., Inc.*, 54 F.3d at 1576 ("The prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution"); *Zenith Labs. v. Bristol-Myers Squibb*, 19 F.3d 1418, 1421 (Fed. Cir.) ("Prosecution history serves as a limit on the scope of claims by excluding any interpretation of the claim language that would permit the patentee to assert a meaning for the claim that was disclaimed or disavowed during prosecution in order to obtain claim allowance"); *see also Alshtrom*

Machinery, Inc. v. Clement, 13 F. Supp.2d 45, 48 n.2 (D.D.C. 1998) ("During the claim construction stage, the prosecution history is … limited to 'exclud[ing] any interpretation that was disclaimed during prosecution") (citation omitted), *aff'd sub nom. Kamyr, Inc. v. Clement*, 217 F.3d 860 (Fed. Cir. 1999).

During Bristol's prosecution of an application related to the '365 patent, "the Patent Examiner rejected Bristol's claim covering the administration of buspirone (rather than the metabolite) as anticipated or, in the alternative, obvious over the prior offer for sale and public use of buspirone, *i.e.*, its administration to patients more than one year before the effective filing date of the application." *See* Mot. for Prelim. Inj. at 7 n.4. As Mylan explains, the Patent Office identified two distinct inventions—the use of BMY 28674 and the use of a prodrug of BMY 28674 (*i.e.*, buspirone). *See* Pl.'s Reply at 12. Bristol was then forced by the Patent Office to choose between these two inventions.[18] *See id*.

Initially, Bristol elected the prodrug subject matter, amending the claim to recite only the use of a prodrug of BMY 28674, but the Patent Office rejected those claims as anticipated by the prior-art use of buspirone to treat anxiety. *See* Pl.'s Reply at 12. In response to this rejection, Bristol chose to prosecute a divisional application directed to the other invention—use of BMY 28674 itself—and again amended the claims, this time to delete reference to a prodrug. *See id.* Bristol then filed a continuation-in-part application adding language to the specification distinguishing the invention over the prior art use of buspirone. *See id.* According to Mylan, "it

[18] Under what is known as a "restriction requirement," a patent claim may contain only a single invention. *See* 35 U.S.C. § 121 (Divisional Applications). "If two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions." *Id*.

was this narrowed claim that Bristol was finally able to gain allowance of in the '365 patent." *Id*. at 12.

Mylan argues that as a matter of law, Bristol cannot recover the prodrug subject matter surrendered by it as a result of the restriction requirement in the parent application. *See* Pl.'s Reply at 12. The Federal Circuit has spoken to this issue, stating that:

> Common sense dictates that a divisional application filed as a result of a restriction requirement may not contain claims drawn to the invention set forth in the claims elected and prosecuted to patent in the parent application. The divisional application must have claims drawn only to the "other invention."

Gerber Garment Tech., Inc. v. Lectra Sys., Inc., 916 F.2d 683, 687 (Fed. Cir. 1990); *see also Spectrum Int'l*, 164 F.3d at 1379 ("a patentee, after relinquishing subject matter to distinguish a prior art reference … 'cannot during subsequent litigation escape reliance [by the defendant] upon this ambiguous surrender of subject matter"); *Zenith Labs. v. Bristol-Myers Squibb Co.*, 19 F.3d at 1421 ("Prosecution history serves as a limit on the scope of claims by excluding any interpretation of the claim language that would permit the patentee to assert a meaning for the claim that was disclaimed or disavowed during prosecution in order to obtain claim allowance"). Thus, Mylan argues, under *Gerber* and its kin, and the prosecution history, the '365 patent cannot claim the administration of buspirone at all. The court finds this argument persuasive.

In its opposition brief, Bristol makes no attempt to reconcile the prosecution history of the '365 patent with its proffered construction of the '365 patent claim. In fact, only during oral argument did Bristol address this issue, referring the court to a document in the prosecution history, dated July 18, 2000, called "Preliminary Communication to the Examiner." *See* Tr. at 37. According to this document, Bristol explained, "it [was] clear that the term 'systemic

administration' appearing in the claim presently before the examiner as defined in the specification specifically includes the oral administration of the buspirone pro-drug form of the metabolite even if the general term pro-drug no longer appears in the claim…. the deletion of the term pro-drug from the claim did not change the scope of the applicant's claimed intention." *Id*. What Bristol did not tell the court, however, was that the Preliminary Communication to the Examiner was part of an application that Bristol expressly abandoned. *See id*. at 60-61.[19] Thus, even at oral argument, Bristol failed to explain why it should not be bound by its surrender of the coverage of the administration of buspirone during the prosecution history.

Accordingly, for the reasons discussed above, and in light of Bristol's failure to rebut many of Mylan's persuasive arguments, the court determines that Mylan has demonstrated a substantial likelihood of success on the merits.

2. Whether Mylan Will Suffer Irreparable Harm if the Injunction is Not Granted

Though Mylan has demonstrated a substantial likelihood of success on the merits, it has failed to establish that it will be irreparably harmed if the court does not grant it injunctive relief. This court has held that "to establish irreparable injury justifying preliminary relief, the plaintiffs must show that the injury is certain, great, and actual, not theoretical; injury must be imminent, creating a clear and present need for equitable relief to prevent harm." *Varicon Int'l v. Office of Personnel*

[19] Even if the Preliminary Communication to the Examiner had not been part of an abandoned application, Bristol would still have to explain the fact that it chose to prosecute a divisional application directed to the other invention—use of the metabolite BMY 28674—and amended its claim to delete reference to the prodrug.

Mgt., 934 F. Supp. 440, 448 (D.D.C. 1996). In addition, Mylan must demonstrate "that the injury [is] more than simply irretrievable; it must also be serious in terms of its effect on the plaintiff." *Gulf Oil Corp. v. Dep't of Energy*, 514 F. Supp. 1019, 1026 (D.D.C. 1981).

Mylan asserts that the FDA's refusal to grant immediate final approval of Mylan's ANDA causes irreparable injury to Mylan. *See* Mot. for Prelim. Inj. at 34. Specifically, Mylan claims that: (1) "it loses revenues for every day that it could be manufacturing and selling its Buspirone Product," *id*.; (2) "if the FDA does not accept Mylan's Section viii Statement, Mylan would be forced to file a Paragraph IV certification and may, as a result, lose its 180 day exclusivity which would have a devastating affect [sic] on Mylan's sales," *id.*; (3) "Mylan has also suffered, and will continue to suffer loss of credibility with its customers as a result of its inability to make promised deliveries," *id.*, and (4) the inevitable drop in stock prices when earnings fall short of expectations may lead to such irreparable harm as employee layoffs and increased vulnerability to a takeover, *see* Pl.'s Reply at 19.

The D.C. Circuit is hesitant to award injunctive relief based purely on lost opportunities and market share. *See Mylan Pharms., Inc. v. Shalala,* 81 F. Supp.2d 30, 42 (D.D.C. 2000); *Berman v. DePetrillo*, 1997 WL 148638, *2 (D.D.C. 1997) ("the loss of a business opportunity is a purely economic injury, and economic loss alone, however substantial, does not constitute 'irreparable harm'"); *see also Barton v. District of Columbia*, ---F. Supp.2d ---, 2001 WL 210102, at *11 (D.D.C. 2001) (Urbina, J.); *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 221 (D.D.C. 1996) (mere speculation about potential market share does not constitute irreparable injury); *Mead Johnson Pharm. Group v. Bowen*, 655 F. Supp. 53, 56 (D.D.C.

1986) (purported loss of market share was "pure speculation"), *aff'd*, 838 F.2d 1332 (D.C. Cir. 1988).

It is true that this court has found irreparable harm where the moving party made a "strong showing that economic loss would significantly damage its business above and beyond a simple diminution in profits." *See Mylan*, 81 F. Supp.2d at 42; *Express One Int'l, Inc. v. United States Postal Serv.*, 814 F. Supp. 87, 91 (D.D.C. 1992) (bidder demonstrated irreparable injury where loss of ten-year $1 billion contract would cause annual loss of $130 million, would impair bidder's relationships with subcontractors and would likely cause capital costs and layoffs); *McGregor Printing Corp. v. Kemp*, 1992 WL 118794, *5 (D.D.C. 1992) ("the irretrievable monetary loss … in combination with the loss in employment to [plaintiff's] employees" amounted to irreparable harm).

In this case, Mylan has not shown that its economic losses would be either "irretrievable" or "would significantly damage its business above and beyond a simple diminution in profits." Mylan claims that it faces a potential loss of $31,250,000 during the next year, or about 13 percent of its projected net earnings for the fiscal year ending March 31, 2001. *See* Pl.'s Reply at 18-19. Mylan does not face the same harm that the plaintiff in *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20 (D.D.C. 1997) would have encountered, where the court found that research and development costs incurred by drug manufacturers were significant in light of the company's small size. *See id.* at 28-29. By contrast, as this court recently observed, "Mylan is

the nation's largest generic drug manufacturer, with annual sales of approximately three-quarters of a billion dollars." *Mylan*, 81 F. Supp.2d at 43.[20]

Mylan also alleges several forms of non-economic injury. Specifically, Mylan alleges that as a result of the drop in stock prices, which inevitably occurs "when earnings fall short of expectations," Mylan will likely suffer "such irreparable harm as employee layoffs or increased vulnerability to a takeover." *See* Pl.'s Reply at 19. Mylan also claims it will suffer a loss of credibility among its customers as a result of its inability to make promised deliveries. *See* Mot. for Prelim. Inj. at 35. Finally, Mylan argues that if the injunction is not granted, it will lose the 180-day period of market exclusivity to which it claims it is entitled for being the first generic producer for this particular product. Since Mylan fails to support these assertions with specific citations to the record, however, its allegations do not rise above the level of mere speculation.

Accordingly, the court determines that Mylan will not suffer irreparable harm if the requested injunction is not granted.

3. Whether the FDA or Bristol-Myers Will Be Injured by the Granting of the Injunction

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[20] Of course, as this court has noted, "these authorities do not stand for the proposition that a generic drug maker never suffers irreparable harm as a result of having one of its products wrongfully kept off the market." *Mylan*, 81 F. Supp.2d at 43. The D.C. Circuit has recognized that generic drug makers "face continued harm [when they are] denied access to the market." *Id.* (citing *Teva Pharms. USA, Inc. v. FDA*, 182 F.3d 1003, 1011 n.8 (D.C. Cir. 1999) (citation omitted)). "The FDA itself has acknowledged that "[e]very day after the tentative approval during which the subsequent applicant can not market its product represents a lost opportunity both for the subsequent applicant and the consumer." *Id.* (citing *180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications*, 64 Fed. Reg. 42,873, 42,878 (1999)).

Any injury to Mylan "must be weighed against … the extent to which an injunction will substantially injure [another] party." *Serono Labs. v. Shalala*, 158 F.3d 1313, 1317-18 (D.C. Cir. 1998). The FDA argues that it will be harmed by a "disruption of its processes for listing patents and resolving disputes related to listed patents if a preliminary injunction is entered." FDA Opp'n at 35. The FDA is correct, but only to a point. Were this court to order the FDA to accept Mylan's Section viii Statement, ANDA holders could disrupt the process for listing patents by unilaterally deciding the scope of a patent, and then imposing their decisions on the FDA. On the other hand, Mylan is likely to prevail on its contention that Bristol improperly submitted its '365 patent to the FDA for listing in the Orange Book. The FDA has already given tentative approval to Mylan's ANDA. If the court allows Mylan's generic buspirone product to assume its rightful place on the market, and not on the loading dock where it currently sits, this order would not frustrate the FDA's mission to protect the public by ensuring that drugs are safe and effective.

Bristol argues that the requested injunction would cause it substantial harm by denying it a period of exclusivity of up to thirty months. *See* Bristol Opp'n at 31. Since Bristol has not shown that it was entitled to this additional period of exclusivity, however, it cannot show that it would be substantially harmed by competition from generic drug makers.

The likely harm to the defendants, then, does not weigh heavily against preliminary injunctive relief. The court therefore concludes that this factor tilts toward the plaintiff.

4. Prong 4: Whether the Public Interest Favors Granting a Preliminary Injunction

The fourth and final part of the preliminary-injunction analysis instructs the court to consider whether the public interest favors the granting of an injunction. The public interest here is multi-faceted: (1) promoting public access to generic buspirone and (2) promoting industry incentives to research and develop new drug treatments. *See Mylan Pharm., Inc. v. Henney*, 94 F. Supp.2d 36, 59 (D.D.C. 2000) (Urbina, J.). This duality is embodied in the Hatch-Waxman Act itself, which strives to induce name-brand pharmaceutical firms to develop new drug products while simultaneously enabling competitors to bring cheaper, generic copies of those drugs to market. Thus, Mylan is only partially correct when it says the legislative goal of the Hatch-Waxman Act is to "make available more low cost generic drugs." *See* Mot. for Prelim. Inj. at 36 (citing H.R. Rep. No. 98-857, pt. 1, 98th Cong., 2d Sess., at 14 (1984)); *see also* Bristol Opp'n at 32-33 ("the legislative goals of the Hatch-Waxman Act ... are not one-sided").

On the other hand, the public interest does not favor a distortion of the principles of the Hatch-Waxman Act. By creating new—and probably impermissible—ways to extend its monopoly, Bristol not only limits the public's access to low-cost drugs, but impedes the very innovation that Hatch-Waxman is designed to promote.

Accordingly, the court determines that the public interest favors the granting of a preliminary injunction to Mylan.

E. Motion for Preliminary Injunction Granted

Mylan has demonstrated a substantial likelihood of success on the merits, possibly the most important factor for preliminary injunctive relief in this Circuit. *See Davenport v. Int'l Bhd. of Teamsters*, 166 F.3d 356, 367 (D.C. Cir. 1999) (absent a showing of likely success on the

merits, "it would take a very strong showing with respect to the other preliminary injunction factors to turn the tide in [the plaintiff's] favor") (citation omitted). Specifically, Mylan has shown a substantial likelihood that this court will issue a declaratory judgment stating that Bristol improperly submitted the '365 patent for listing in the Orange Book. Although Mylan failed to demonstrate that it would suffer irreparable harm, Mylan has demonstrated that the public interest favors granting the injunction, and that the balance of harms to the parties does not weigh against granting the injunction. Accordingly, since Mylan makes such a strong showing on three of the four preliminary-injunction factors, the court concludes that Mylan has met the stringent standard for obtaining a mandatory preliminary injunction.

VI. CONCLUSION

For the foregoing reasons, the court orders as follows:

Defendant Bristol-Myers Squibb Co. is hereby enjoined to request that Defendant FDA delist U.S. Patent No. 6,150,365 from its publication "Approved Drug Products with Therapeutic Equivalence Evaluations" (also known as the "Orange Book"), that is, Bristol is directed to request the FDA to remove its '365 patent from the Orange Book; and

Defendant Tommy G. Thompson, the United States Food and Drug Administration, and their agents, servants and employees are hereby ordered to grant immediate approval of Mylan's abbreviated new drug application (ANDA) No. 75-272 to market its pharmaceutical product containing buspirone hydrochloride as a generic version of BuSpar®.

An Order directing the parties in a manner consistent with this Memorandum Opinion is separately and contemporaneously executed this _____ day of March 2001.

_____

Ricardo M. Urbina
United States District Judge

UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF COLUMBIA

MYLAN PHARMACEUTICALS, INC., Plaintiff, v. TOMMY G. THOMPSON, Secretary, United States Department of Health and Human Services, United States Food and Drug Administration, and BRISTOL-MYERS SQUIBB CO., Defendants.	Civil Action No.: 00-2876 (RMU) Document Nos.: 3, 4

O R D E R

GRANTING THE PLAINTIFF'S MOTION FOR PRELIMINARY INJUNCTION

Upon consideration of the plaintiff's motion for preliminary injunction, the defendants' opposition thereto, and the entire record herein, and for the reasons stated in the Memorandum Opinion issued separately and contemporaneously with this Order,

it is this ____ day of March 2001,

ORDERED that Defendant Bristol-Myers Squibb Co. is hereby enjoined to request that Defendant FDA delist U.S. Patent No. 6,150,365 from its publication "Approved Drug Products

with Therapeutic Equivalence Evaluations" (also known as the "Orange Book"), that is, Bristol is directed to request the FDA to remove its '365 patent from the Orange Book; and it is

FUTHER ORDERED that Defendant Tommy G. Thompson, the United States Food and Drug Administration, and their agents, servants and employees grant immediate approval of Mylan's abbreviated new drug application (ANDA) No. 75-272 to market its pharmaceutical product containing buspirone hydrochloride as a generic version of BuSpar®.

SO ORDERED.

Ricardo M. Urbina

United States District Judge